REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed, although claims 27, 29, 38, 40 and 43 are only objected to as being dependent upon a rejected base claim, but would otherwise be allowable if rewritten in independent form. Claims 1-15, 27, 29 and 42-58 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The personal interview among Mr. Browdy and Mr. Yun, representing applicant, and Examiners Emch and Kemmerer on May 13, 2008, is hereby gratefully acknowledged. Applicant's representatives wish to thank the examiners for the courtesies extended during this interview. The arguments presented at the interview are incorporated into the remarks below.

Claims 1-11, 13-15, 42, 44-46 and 49 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Schenk et al., WO 00/72880. The examiner states that Schenk teaches that immunogenic fragments of Aβ are advantageous for therapeutic use and can be presented by a display vehicle as part of an immunogenic composition, citing page 14, line 19, to page 16, line 17. The examiner further states that this segment of the document also teaches that the fragments

require screening before use and asserts that this is exactly what is being performed in Figures 19-20, i.e., the peptides are being screened. The examiner takes the position that the skilled artisan would know that the peptides need not be used only in an assay for epitope mapping. This rejection is respectfully traversed.

Claim 1 has now been amended to recite "an antigenic product which induces an immune response against an epitope that spans the β-secretase cleavage site of amyloid precursor protein (AβPP)". The incorporation into claim 1 of language reciting an epitope that spans the β-secretase cleavage site of AβPP was discussed with the examiners at the May 13, 2008, interview. This language is supported by the specification, for example at page 16 lines 21-26.

Before proceeding to discuss this amendment insofar as it relates to this §103(a) rejection over Schenk, applicant wishes to address the previous §102(b) rejection over the Schenk reference that was withdrawn in view of the previous amendment to claim 1 to recite a 6-14 amino acid residue peptide. Claim 1, as amended here, no longer recites the feature of a 6-14 amino acid residue AβPP epitope. However, the 104 residue pBx6 polypeptide disclosed on pages 62-68 of Schenk simply cannot anticipate or make obvious the presently

claimed invention. Schenk clearly discloses on page 68, lines 1-3:

> Lack of T-cell and low antibody response from fusion peptide pBx6, encompassing APP amino acids 592-695 including all of the Aβ residues may be due to the poor immunogenicity of this particular preparation.

Therefore, the pBx6 polypeptide, which not only includes all the Aβ residues but also the β-secretase cleavage site, does not satisfy the requirement of presently amended claim 1 that the immunizing composition comprises an immunizing effective amount of an antigenic product which induces an immune response against an epitope that spans the β-secretase cleavage site of AβPP (APP). As the pBx6 polypeptide does not induce an immune response, Schenk's disclosure and teaching of this pBx6 polypeptide do not meet the recited features of the present claims. Moreover, one of ordinary skill in the art would have no motivation to use the pBx6 polypeptide in an immunizing composition of the present invention in the face of Schenk's teaching of the lack of any substantial T-cell and antibody response to pBx6.

Turning back to the instant rejection, it should be emphasized that Schenk's invention and its teachings, like many others in the field of therapeutics for Alzheimer's disease, are solely directed to using the peptides and

epitopes of Aβ (beta-amyloid) to raise antibodies against Aβ. Nowhere in Schenk is there any suggestion to use peptides and epitopes other than from Aβ to immunize and treat Alzheimer's disease. Accordingly, while applicant agrees with the examiner's statement that immunogenic fragments of Aβ are advantageous for therapeutic use against Alzheimer's, applicant disagrees with the examiner's position that it would be obvious to use all the peptides illustrated in Figures 19-20 in immunogenic compositions to treat Alzheimer's. The peptides used in the experiment illustrated by Figs. 19-20 were only generated to map the epitopes recognized by antibodies raised against AN1792 (Aβ1-42; see pages 101-104 of Schenk).

Certainly, the peptides in Figures 19-20 are not screened for immunogenicity; rather, they are screened to map the epitopes that would be bound by antibodies raised against Aβ. The examiner states at page 12 of the Office Action of January 17, 2008, "The skilled artisan would know that the peptides need not be used only in an assay for epitope mapping." However, while this may be true for peptides that are fragments of Aβ, it is not true for those peptides illustrated in Figs. 19-20 that are not fragments of Aβ. The examiner states at page 12, lines 6-8, of the same Office Action that "Schenk teaches that immunogenic fragments of Aβ

are advantageous for therapeutic use." This is true. But Schenk does not teach that peptides that are not fragments of Aβ could be advantageous for the therapeutic use. The peptides used in the present invention must span the β-secretase cleavage site. It is emphasized that none of the epitopes spanning the β-secretase cleavage site are fragments of Aβ because any such epitope must contain residues of AβPP that do not appear in Aβ. Thus, it would not have been obvious to one of ordinary skill in the art to use any peptides of Figures 19-20 that are not fragments of Aβ (i.e., any of the first eight listed peptides in Fig. 19) in an immunogenic composition for Schenk's purpose of raising antibodies against Aβ for treating Alzheimer's disease. In other words, while these particular peptides may be useful for epitope mapping, they would not be considered to be useful for immunological screening. Therefore, there would have been no motivation to remove them from the bound substrate and use them in an immunological assay.

While the present invention also seeks to treat Alzheimer's disease, it uses a completely different approach. In the present invention, antibodies are raised against an epitope that spans the β-secretase cleavage site (an epitope that cannot be present in Aβ), and not epitopes and peptides

only from Aβ. Schenk only teaches raising antibodies against an epitope of Aβ, which epitope cannot be present in an epitope that spans the β-secretase cleavage site. Accordingly, Schenk cannot lead one of ordinary skill in the art to the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 11 and 12 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Schenk et al., WO 00/72880, in view of Frenkel et al., *Proc. Natl. Acad. Sci. USA* 97(21):11455-11459 (2000). The Schenk reference is being applied as above in the preceding obviousness rejection. Frenkel is applied for its teaching of filamentous bacteriophages useful for immunization procedures. This rejection is respectfully traversed.

Claims 11 and 12 are ultimately dependent from claim 1. Therefore, the deficiencies of Schenk as discussed above in the preceding obviousness rejection apply to this rejection as well. Frenkel's teaching of filamentous bacteriophage useful for immunization does not fulfill any of the deficiencies of Schenk. Frenkel does not teach use of any epitope that spans the β-secretase cleavage site. Accordingly, the combination of Schenk and Frenkel cannot lead one of ordinary skill in the art to the subject matter of

claims 11 and 12. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-3, 5-10, 15, 44-47, 49 and 50 have been provisionally rejected for nonstatutory obviousness-type double patenting over claims 1-2, 6, 10, 16-17 and 21-24 of copending application no. 10/481,642. The examiner takes the position that the skilled artisan would recognize that administration of an immunizing composition comprising VKMDAEFRH (SEQ ID NO:5) would produce a polyclonal antibody response comprising antibodies directed not only to the β-secretase cleavage site as instantly claimed, but also to the highly antigenic portion of amyloid β, particularly to the EFRH epitope. This rejection is respectfully traversed.

The claims of US'642 are directed to antigenic products that display an epitope of Aβ. Thus, similar to the cited and applied Schenk reference, there is simply no suggestion or motivation to include epitopes that are not part of Aβ. The examiner's position that one of ordinary skill in the art would recognize that VKMDAEFRH would raise not only antibodies to Aβ but also to the β-secretase cleavage site is irrelevant, even if one were to assume it is true, which is not necessarily the case. The issue is one of obviousness. As with the Schenk reference, discussed above, there would simply be no reason for one of ordinary skill in the art to

use an epitope that spans the β-secretase cleavage site when the goal of US'642 is to raise antibodies to the deposit-forming peptide, i.e., Aβ.

Merely because the claims of US'642 "dominates" the claims of the present application, i.e., by a small overlap in a Venn diagram, (or *vice versa*) does not mean that there is double patenting. MPEP 804 II states:

> Domination and double patenting should not be confused. They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. Domination by itself, i.e., in the absence of statutory or nonstatutory double patenting grounds, cannot support a double patenting rejection. *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964). However, the presence of domination does not preclude double patenting. See, e.g., *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968).

Even if the claims of US'642 would be considered to "dominate" the present claims, i.e., be broad enough to read on the use of the peptide of SEQ ID NO:5 of the present application, they do not make obvious the presently claimed invention. There would be no motivation to one of ordinary skill in the art reading the claims of the present invention to use any of the

epitopes set forth in such claims for the purpose of US'642. Furthermore, if they were used, unexpected results would occur because antibodies would be raised not only against Aβ, but also against the β-secretase cleavage site (according to the examiner's hypothesis, which has not been proved). Were this to happen, one would get the advantages of US'642 as well as the separate and distinct advantages of the present invention. The cumulative effect would have been unobvious to one of ordinary skill in the art reading only US'642. The inventions are different and, even if they overlap, would not be obvious one over the other. Accordingly, reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 11, 12 and 14 have been provisionally rejected under the doctrine of nonstatutory obviousness-type double patenting over claims 1, 3 and 10 of copending application no. 11/073,526. The examiner states that this is similar to the situation above with respect to US'642 because the polypeptide displayed on the virus particle comprises at least one epitope of amyloid β. This rejection is respectfully traversed.

Similar to the argument presented above, US'526 is directed to a virus particle displaying a peptide which includes epitopes of amyloid β to induce an immune response to

amyloid β. Such a virus particle may optionally include other residues besides those in an epitope of amyloid β. However, any such additional residues would include the β-secretase cleavage site merely by coincidence and not by design. Thus, one of ordinary skill in the art would not be motivated to specifically include residues from the β-secretase cleavage site in AβPP that are not present in amyloid β on a virus particle (to be displayed with the amyloid β epitope) when the goal of US'526 is to elicit an immune response against the amyloid β target, not the β-secretase cleavage site of AβPP.

As with the preceding obviousness-type double patenting rejection, while the claims of US'526 may "dominate" the present claims, they do not make obvious the presently claimed invention without the benefit of hindsight. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Applicant is filing on even date herewith an Information Disclosure Statement listing applicant's own issued patents and published applications in the field of Aβ and treating Alzheimer's. However, just as the two copending applications applied in the above obviousness-type double patenting rejections may "dominate" the present application,

the references listed in this IDS do not make obvious the presently claimed invention.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /ACY/
Allen C. Yun
Registration No. 37,971

ACY:pp
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\R\ramq\Solomon6A\PTO\2008-05-19amendment.doc